

CLAIMS

1. A method for facilitating the termination of cell signalling by a cytokine or cytokine-like molecule, said method comprising promoting interaction between a SOCS-box-containing peptide, polypeptide or protein or a chemical analogue thereof and one or more other molecules wherein the resulting complex is subjected to degradation *via* the ubiquitination or proteasomal compartments.
2. Use of a SOCS-box-containing peptide, polypeptide or protein or a chemical analogue thereof together with one or more other molecules to couple said SOCS-box-containing peptide, polypeptide or protein and/or one or more other molecules to the ubiquitination or proteasomal compartments thereby terminating or substantially reducing cytokine- or cytokine-like molecule-mediated cell signalling.
3. A method according to Claim 1 or 2 wherein the one or more other molecules are elongin B and/or elongin C.
4. A method according to Claim 1 or 2 wherein the one or more other molecules are selected from elongin B, elongin C, elongin A or VHL or combinations of elongin B, C and/or A, and/or VHL.
5. A method according to claim 1 wherein said peptide, polypeptide or protein or a chemical analogue thereof is encoded by a sequence of nucleotides encoding the amino acid sequence:-

$$X_1 X_2 X_3 X_4 X_5 X_6 X_7 X_8 X_9 X_{10} X_{11} X_{12} X_{13} X_{14} X_{15} X_{16} [X_i]_n X_{17} X_{18} X_{19} X_{20}$$

$$X_{21} X_{22} X_{23} [X_j]_n X_{24} X_{25} X_{26} X_{27} X_{28}$$

wherein: X_1 is L, I, V, M, A or P;
 X_2 is any amino acid residue;

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X_3 is P, T or S;

X_4 is L, I, V, M, A or P;

X_5 is any amino acid;

X_6 is any amino acid;

X_7 is L, I, V, M, A, F, Y or W;

X_8 is C, T or S;

X_9 is R, K or H;

X_{10} is any amino acid;

X_{11} is any amino acid;

X_{12} is L, I, V, M, A or P;

X_{13} is any amino acid;

X_{14} is any amino acid;

X_{15} is any amino acid;

X_{16} is L, I, V, M, A, P, G, C, T or S;

$[X_i]_n$ is a sequence of n amino acids wherein n is from 1 to 50 amino acids and wherein the sequence X_i may comprise the same or different amino acids selected from any amino acid residue;

X_{17} is L, I, V, M, A or P;

X_{18} is any amino acid;

X_{19} is any amino acid;

X_{20} L, I, V, M, A or P;

X_{21} is P;

X_{22} is L, I, V, M, A, P or G;

X_{23} is P or N;

$[X_j]_n$ is a sequence of n amino acids wherein n is from 0 to 50 amino acids and wherein the sequence X_j may comprise the same or different amino acids selected from any amino acid residue;

X_{24} is L, I, V, M, A or P;

X_{25} is any amino acid;

X_{26} is any amino acid;

X_{27} is Y or F;

X₂₈ is L, I, V, M, A or P.

6. An agonist or antagonist of cytokine- or cytokine-like molecule-mediated cell signalling, said agonist or antagonist facilitating or otherwise promoting or reducing or otherwise preventing complex formation between two or more of:-
 - (i) a SOCS-box-containing peptide, polypeptide or protein or functional equivalent thereof or chemical analogue thereof;
 - (ii) elongin B and/or C or functional equivalents thereof or chemical analogues thereof; and/or
 - (iii) elongin A and/or VHL or functional equivalents thereof or chemical analogues thereof.
7. An agonist or antagonist according to Claim 6 wherein said agonist or antagonist is an isolated, naturally occurring molecule.
8. A method of modulating activity of SOCS in a human, said method comprising administering to said mammal an effective amount of a molecule for a time and under conditions sufficient to increase or decrease elongin B and/or elongin C binding to a SOCS box.
9. A method of modulating levels of a SOCS protein in a cell said method comprising contacting a cell containing a SOCS gene with an effective amount of an inhibitor of elongin B- and/or elongin C- interaction with a SOCS box encoded by said SOCS gene for a time and under conditions sufficient to modulate levels of said SOCS protein.
10. A method of modulating signal transduction in a cell containing a SOCS gene comprising contacting said cell with an effective amount of an inhibitor of elongin B and/or elongin C interaction with a SOCS box encoded by said SOCS gene for a time sufficient to modulate levels of SOCS protein with the cell.

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11. Use of one or more of:-

- (i) elongin B or a functional equivalent or chemical analogue thereof;
- (ii) elongin C or a functional equivalent or chemical analogue thereof;
- (iii) elongin A or a functional equivalent or chemical analogue thereof;
- (iv) VHL or a functional equivalent or chemical analogue thereof;
- (v) a peptide, polypeptide or protein comprising a SOCS box ;
- (vi) an agonist or antagonist of one or more of (i) - (v);
- (vii) an agonist or antagonist of a complex formed by two or more of (i) to (v);
- (viii) a chemical analogue or derivative of one or more of (i) - (vii);

in the manufacture of a medicament in the treatment of a condition in a subject.

12. A genetically modified animal comprising a mutation in genetic material encoding a SOCS-box-containing protein such that said SOCS-box in said SOCS-box containing protein is not capable of functionally interacting with one or more of elongin A, B or C, VHL or a cytokine or cytokine-like molecule.

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